

## SEQUENCE LISTING

<120> ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES THEREOF

<130>	28341/6280NCP	R	ECEIVE	Đ		
	US 09/668,314 2000-09-22		UN 1 9 2002	_		
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aaaa					1804

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Met Gly Ala Leu Ala Arg Ala Leu Leu Leu Pro Leu Leu Ala Gln Trp
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<sup>&</sup>lt;211> 518

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 2

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- Leu Arg Val Ala Ala Ala Thr Asn Arg Val Val Ala Pro Thr Pro Gly 35 40 45
- Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu Ala Leu Ala Leu 50 55 60
- Glu Pro Ala Leu Ala Ser Pro Ala Gly Ala Ala Asn Phe Leu Ala Met 70 75 80
- Val Asp Asn Leu Gln Gly Asp Ser Gly Arg Gly Tyr Tyr Leu Glu Met 85 90 95
- Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp Thr Gly 100 105 110
- Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile Asp Thr 115 120 125
- Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly Phe Asp 130 135 140
- Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val Gly Glu 145 150 155 160

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- Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu Val Asn 165 170 175
- Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly Ile Lys
  180 185 190
- Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys Pro Ser 195 200 205
- Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile 210 215 220
- Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala 225 230 235 240
- Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro 245 250 255
- Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp 260 265 270

Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met . 375 Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser Glu Pro Ile Leu Trp Ile Val Ser Tyr Ala Leu Met Ser Val Cys Gly Ala Ile Leu Leu Val Leu Ile Val Leu Leu Leu Pro Phe Arg Cys Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu Ser Ser Leu Val Arg His Arg Trp Lys

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<211> 501

<212> PRT

<213> Homo sapiens

<400> 4

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Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp 35 40 45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val 50 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 150 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp 165 170 175

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Ser	Leu	Glu 195	Pro	Phe	Phe	Asp	Ser 200	Leu	Val	Lys	Gln	Thr 205	His	Val	Pro
Asn	Leu 210	Phe	Ser	Leu	Gln	Leu 215	Cys	Gly	Ala	Gly	Phe 220	Pro	Leu	Asn	Gln
Ser 225	Glu	Val	Leu	Ala	Ser 230	Val	Gly	Gly	Ser	Met 235	Ile	Ile	Gly	Gly	Ile 240
Asp	His	Ser	Leu	Tyr 245	Thr	Gly	Ser	Leu	Trp 250	Tyr	Thr	Pro	Ile	Arg 255	Arg
Glu	Trp	Tyr	Tyr 260	Glu	Val	Ile	Ile	Val 265	Arg	Val	Glu	Ile	Asn 270	Gly	Gln
Asp	Leu	Lys 275	Met	Asp	Cys	Lys	Glu 280	Tyr	Asn	Tyr	Asp	Lys 285	Ser	Ile	Val
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Gly	Phe	Trp	Leu	Gly 325	Glu	Gln	Leu	Val	Cys 330	_	Gln	Ala	Gly	Thr 335	Thr
Pro	Trp	Asn	Ile 340	Phe	Pro	Val	Ile	Ser 345	Leu	Tyr	Leu	Met	Gly 350	Glu	Val
Thr	Asn	Gln 355	Ser	Phe	Arg	Ile	Thr 360	Ile	Leu	Pro	Gln	Gln 365	Tyr	Leu	Arg
Pro							Ser		_	_	_		Lys	Phe	Ala
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Gly	Phe	Tyr	Val	Val 405	Phe	Asp	Arg	Ala	Arg 410	Lys	Arg	Ile	Gly	Phe 415	Ala
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Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro 435 440 445 .

Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala 450 460

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp 465 470 . 475 480

Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp 495

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<210> 6

<211> 476

<212> PRT

<213> Homo sapiens

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Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp 35 40 45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val 50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

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Tyr	Val 130	Pro	Tyr	Thr	Gln	Gly 135		Trp	Glu	Gly	Glu 140	Leu	Gly	Thr	Asp
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Ala	Ala	Ile	Thr	Glu 165	Ser	Asp	Lys	Phe	Phe 170	Ile	Asn	Gly	Ser	Asn 175	Trp
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Ser	Met 210	Ile	Ile	Gly	Gly	Ile 215	Asp	His	Ser	Leu	Tyr 220	Thr	Gly	Ser	Leu
Trp 225	Tyr	Thr	Pro	Ile	Arg 230	Arg	Glu	Trp	Tyr	Tyr 235	Glu	Val	Ile	Ile	Val 240
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Ser	Thr 290	Glu	Lys	Phe	Pro	Asp 295	Gly	Phe	Trp	Leu	Gly 300	Glu	Gln	Leu	Val
Cys 305	Trp	Gln	Ala		Thr 310		Pro	Trp		Ile 315	Phe	Pro	Val	Ile	Ser 320
Leu	Tyr	Leu	Met	Gly 325	Glu	Val	Thr	Asn	Gln 330	Ser	Phe	Arg	Ile	Thr 335	Ile
Leu	Pro	Gln	Gln 340	Tyr	Leu	Arg	Pro	Val 345	Glu	Asp	Val	Ala	Thr 350	Ser	Gln
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Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala 370 380

Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu 385 390 395 400

Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu 405 410 415

Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr 420 425 430

Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu 435 440 445

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His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys 465 470 475

<210> 7

<211> 2043

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<sup>&</sup>lt;210> 8

<400> 8

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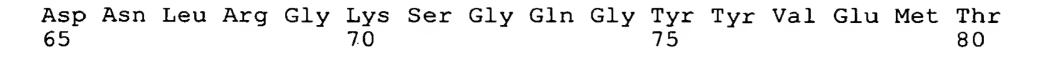
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Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
50 60

<sup>&</sup>lt;211> 501

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Mus musculus



Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 150 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro 195 200 205

Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 215 220

Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 245 250 255

Glu Trp Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 275 280 285

Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala 290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp 305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr 325 330 335 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 340 345 350 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg 355 360 365 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 370 375 380 Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu 385 390 395 400 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 405 410 415 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 420 425 430 Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro 435 440 445

450 455 460

Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp465470475480

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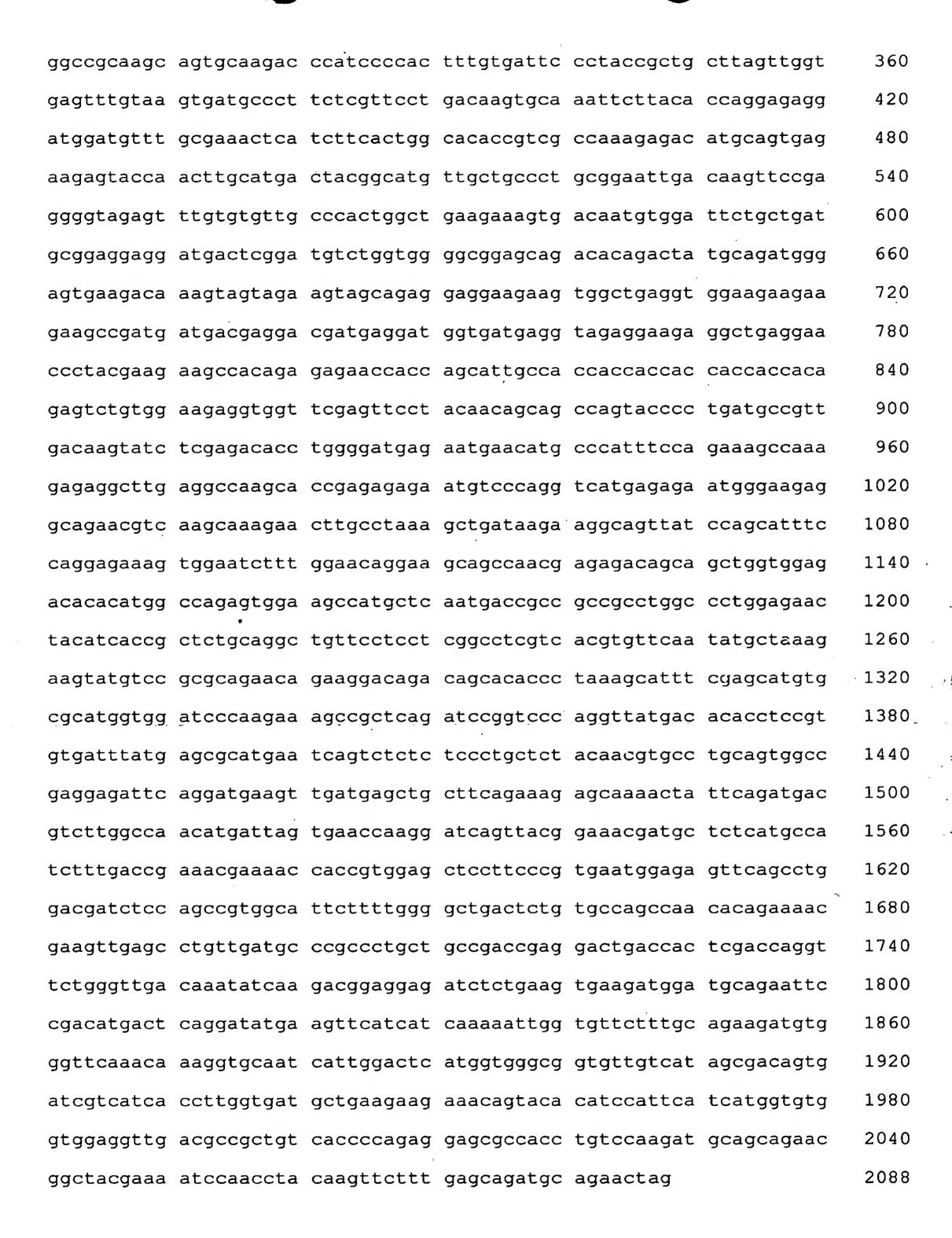
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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu Glu Ala Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala 

.

Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn 485 490 495

Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser 500 510

Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr 515 520 525

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln 530 540

Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn 545 550 560

Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr 565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser 580 585

Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val 595 600 605

His His Glm Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys 610 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val 625 630 635 640

Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr Ser Ile 645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg 660 665 670

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu 225 230 235 240

Glu Ala Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu 245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile 260 265 270

Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg 275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu 290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys 305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg 325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Prō Lys Ala Asp 340 345 350

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu 355 360 365

Gln Glu Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala 370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn 385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe 405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His 420 425 430

Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala 435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu 450 455 460 Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys 0 Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg 

His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys

Phe Phe Glu Gln Met Gln Asn 690 695

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35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Vai Tyr Pro Glu Leu 65 75 80

Gin Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val 100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile 165 170 175 Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu 225 230 235 240

Glu Ala Asp Asp Glu Asp Asp Glu Asp Glu Asp Glu Val Glu Glu 255 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile 260 265 270

Ala Thr Thr Thr Thr Thr Thr Giù Ser Val Glu Glu Val Val Arg 275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu 290 295 300

Glu Thr Pro Gly Asp Glu Asa Glu His Ala His Phe Gln Lys Ala Lys 305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg 325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp 340 345 350

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu 355 360 365

Gln Glu Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala 370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn 385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe 405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His 420 425 430 Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala 435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu 450 455 460

Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala 465 470 475 480

Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn 485 490 495

Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser 500 510

Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr 515 520 525

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln 530 540

Pro Trp His Ser Phe Ĝly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn 545 550 560

Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr 565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asr Ile Lys Thr Glu Glu Ile Ser 580 590

Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val 595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys 610 620

Gly Ala Ile Ile Gly Leu Met Val Glŷ Gly Val Val Ile Ala Thr Val 625 630 635 640

Ile Phe Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile 645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg 660 665 670

His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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1620

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile 165

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu 225 230 235 240

Glu Ala Asp Asp Glu Asp Asp Glu Asp Glu Asp Glu Val Glu Glu 255 250

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
-260 265 270

Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu 290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys 305 310 315 320

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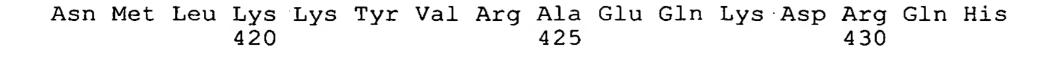
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Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr Ser Ile 645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg 660 665 670

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Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

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Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn

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Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile

## His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg 660 670

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 90 95

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Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu 225 230 235 240

Glu Ala Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu 245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile 260 265 270

Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg 275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu 290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys 305 310 315 320

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Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg 35 40 45

Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly 50 60

Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly 65 75 80

Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile 85 90 95

Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His 100 105 110

Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg 115 120 125

Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu 130 135 140

Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val 145 150 155 160

Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe 165 170 175

Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu 180 185 . 190

Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val 195 200 205

Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu His Leu Cys Gly Ala 210 215 220

Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser 225 230 235 240

Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp 245 250 255

Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg 260 265 270

Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr 275 280 285	Asn
Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu 290 295 300	Pro
Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser 305 310 315	Ser 320
Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val 325 330 335	Cys
Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser 340 345 350	Leu
Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile 355 360 365	Leu
Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln 370 380	Asp .
Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val 1 385 390 395	Met 400
Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala 405 410 415	Arg
Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu 420 425 430	Phe ;
Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu . 435 440 445	Asp
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Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg 35 40 45

Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro 50 60

Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala 65 70 75 80

<sup>/&</sup>lt;211> 433

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

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Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu

205

\* J**\*** 

200

195

Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu 210 215 220

Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr 225 230 235 240

Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met 245 250 255

Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr 260 270

Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser 275 280 285

Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu 290 295 300

Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile 305 310 315 320

Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser 325 330 335

Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp
			340					345					350		

Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser 355 360 365

Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val 370 380

Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys 385 390 395 400

His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val
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Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu 420 425 430

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\*\* =

1/2

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ccagtggaag atgtggccac	gtcccaagac	gactgttaca	agtttgccat	ctcacagtca	1080
tccacgggca ctgttatggg	agctgttatc	atggagggct	tctacgttgt	ctttgatcgg	1140
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Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr 35 40 45

Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val 50 55 60

Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe 65 70 75 80

Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu 90 95

Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu
100 105 110

Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val 115 120 125

Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn 130 135 140

Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala 145 150 150 160

Arg Pro Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp. Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala 'Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly 

Tyr Asn Ile Pro Gln Thr Asp Glu Ser 420 425

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PRT Homo sapiens

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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser 20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp 35 40 45

Glu Glu Pro Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 150 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro 195 200 205

Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 225 230 235 240 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 275 280 285

Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala 290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp 305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr 325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg 355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 370 380

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1

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Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 420 425 430

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Gln Thr Asp Glu Ser 450

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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser 20 25 30

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 32

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Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
50 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro 195 200 205

Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 245 250 255

Glu Trp Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 275 280 285 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala 290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp 305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr 325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg 355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 370 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu385390395400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
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Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro 435 440 . 445

Gln Thr Asp Glu Ser His His His His His 450 455

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<211> 25

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Ser Ser Leu Val Arg His Arg Trp Lys 20 25

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Leu Leu l	Lys							
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		ens						* <u>.</u>  
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Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
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Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 150 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
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Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Leu Cys Gly 180 185 190

Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly
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Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu 210 215 220

Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val 225 230 235 240

Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr 245 250 255

Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu 260 265 270

Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser 275 280 285 Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val 290

Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser 305 310 315 320

Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile 325 330 335

Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln 340 345 350

Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val 355 360 365

Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala 370 375 380

Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu 385 390 395 400

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Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
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Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln

Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val

Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala 370 375 380

Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu 385 390 395 400

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- يا لمين

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Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln 35 40 45

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<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 220 .

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu 225 230 235 240

Glu Ala Asp Asp Glu Asp Asp Glu Asp Glu Asp Glu Val Glu Glu 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile 260 265 270

Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile 290 295 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Met Ser Gln Ser Leu Leu Lys Thr Thr Gln Glu Pro Leu Ala Arg Asp Pro Val Lys Leu Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp 

بالميت ا

Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val 565 570 575

Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala 580 585 590

Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro 595 600 605

Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe 610 620

Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val 625 630 635 640

Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser 645 650 655

Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp 660 665 670

Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu 675 680 685

Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly 690 700

Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu 705 710 715 720

Val Met Leu Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val 725 730 735

A J

Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met 740 745 750

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Gln Asn 770

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 -- 60 --

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val 100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu Glu Ala Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln 

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. :<u>:</u> :

Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe

Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn Glu Arg Gln
420 425 430

Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp 435 440 445

Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu Gln Ala Val 450 455 460

Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys Tyr Val Arg 465 470 480

Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe Glu His Val 485 490 495

Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met 500 505 510

Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser Leu Ser Leu 515 520 525

Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp Glu Val Asp 530 540

Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val Leu Ala Asn 545 550 550 560

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Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro Val Asn Gly 580 590

Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe Gly Ala Asp 595 600 605

Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val Asp Ala Arg 610 620

Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr 625 630 635 640

Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe 645 650 655

Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe 660 670

Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val 675

Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu Val Met Leu 690 695 700

Lys Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val Glu Val Asp 705 710

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

<sup>&</sup>lt;211> 772

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 59

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Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe

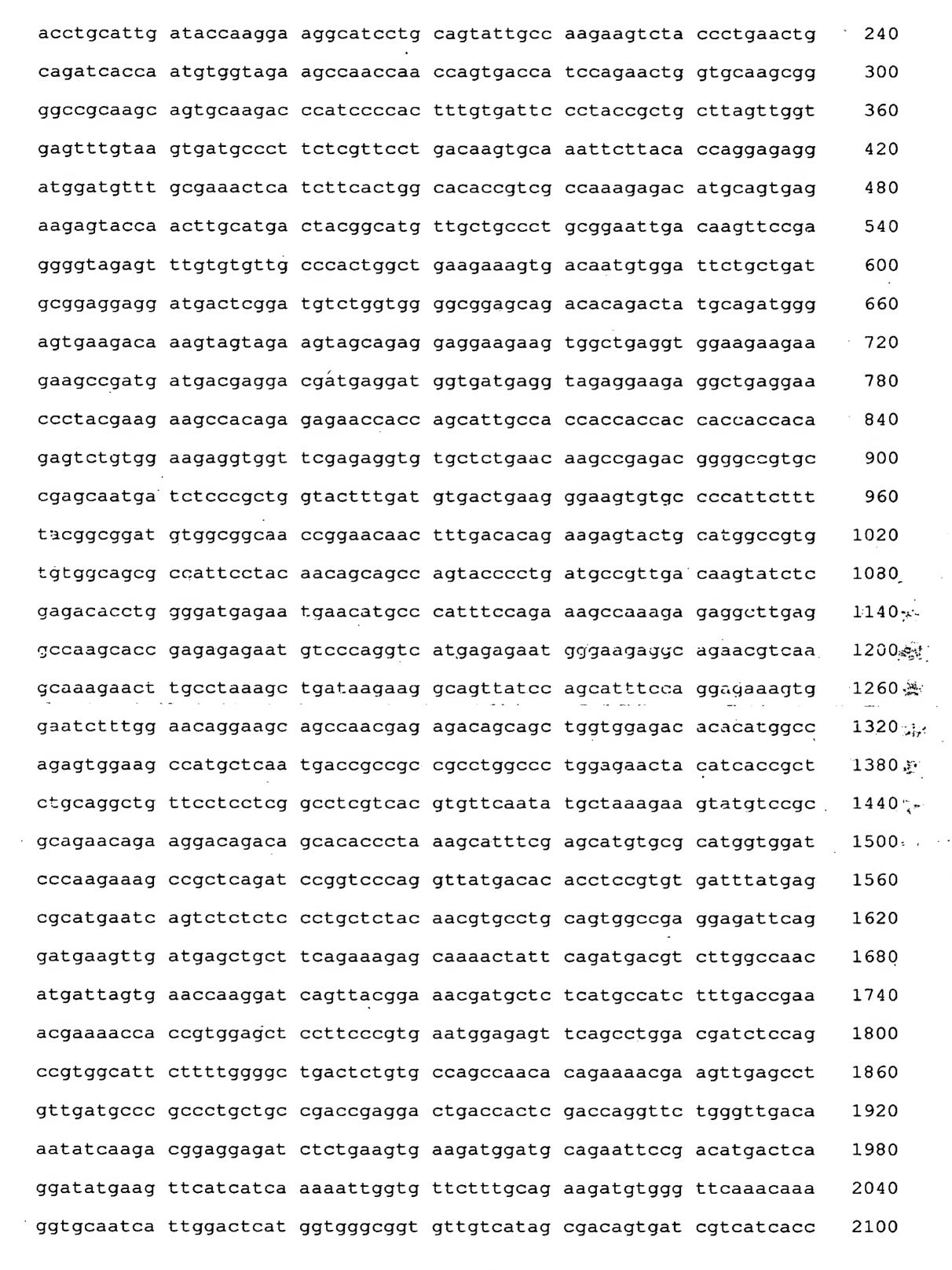
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•																	
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Leu	Met	Pro 595	Ser	.Leu	Thr	Glu	Thr 600	Lys	Thr	Thr	Val	Glu 605	Leu	Leu	Pro		
Val	Asn 610	Gly	Glu	Phe	Ser	Leu 615	Asp	Asp	Leu	Gln	Pro 620	Trp	His	Ser	Phe		•
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Asp	Ala	Arg	Pro	Ala 645	Ala	Asp	Arg	Gly	Leu 650	Thr	Thr	Arg	Pro	Gly 655	Ser		
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Val	Phe 690	Phe	Ala	Glu	Asp	Val 695	Gly	Ser	Asn	Lys	Gly 700	Ala	Ile	Ile	Gly	) •	,
Leu 705	Met	Val	Gly	Gly	Val 710	Val	Ile	Ala	Thr	Val 715	Ile	Val	Ile	Thr	Leu 720		Ħ.
Val	Met	Leu	Lys	Lys 725	Lys	Gln	Tyr	Thr	Ser 730	Ile	His	His	Gly	Val 735	Val		a - Ç4
Glu	Val	Asp	Ala 740	Ala	Val	Thr	Pro	Glu 745	Glu	Arg	His	Leu	Ser 750	Lys	Met .		· ms is
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120



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Glu Thr His Le	ı His Trp His 150	•	Lys Glu Thr Cys 155	s Ser Glu 160								
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Asp Lys Phe Ar	<del>-</del>	Phe Val Cys 185	Cys Pro Leu Ala 190									

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Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 215 220

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Cys Met Ala Val Cys Gly Ser Ala Ile Pro Thr Thr Ala Ala Ser Thr 340 345 350

Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp Glu Asn Glu 355 360 365

His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg 370 375 380

Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln 385 390 395 400

Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe 405 410 415

Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn Glu Arg Gln 420 425 430

Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp 435 440 445 Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu Gln Ala Val 450 455 460

Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys Tyr Val Arg 465 470 475 480

Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe Glu His Val 485 490 495

Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met 500 505 510

Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser Leu Ser Leu 515 520 525

Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp Glu Val Asp 530 540

Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val Leu Ala Asn 545 550 555 560

Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala Leu Met Pro 565 570 575

Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro Val Asn Gly.
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Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe Gly Ala Asp
595 600 605

Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val Asp Ala Arg 610 620

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Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr 625 630 635 640

Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe 645 650 655

Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe 660 670

Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val 675 680 685

Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu Val Met Leu 690 695 700

Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val Glu Val Asp 705 710 715 Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met Gln Gln Asn 725 730 Gly Tyr Glu Asn Pro Thr Tyr Lys Phe Phe Glu Gln Met Gln Asn Lys 740 745 750 Lys <210> 62 <211> <212> PRT <213> Artificial sequence <220> <223> Synthetic peptide <400> 62 Leu Glu Val Leu Phe Gln Gly Pro-

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Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu Ala Leu Ala Leu 50 55 60

Glu Pro Ala Leu Ala Ser Pro Ala Gly Ala Ala Asn Phe Leu Ala Met
70 75 80

A. A.

- -

Val Asp Asn Leu Gln Gly Asp Ser Gly Arg Gly Tyr Tyr Leu Glu Met 85 90 95

Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp Thr Gly 100 105 110

Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile Asp Thr 115 120 125

Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly Phe Asp 130 135 140

Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val Gly Glu
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Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu Val Asn 165 170 175

Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly Ile Lys 180 185 190 Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys Pro Ser 195 200 205

Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile 210 215 220

Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala 225 230 235 240

Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro 245 250 255

Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp
260 265 270

Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu 275 280 285

Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser 290 295 300

Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val 305 310 315 320

Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe
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Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser 355 360 365

Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met 370 380

Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro 385 390 395 400

Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr 405 410 415

Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro 420 425 430

Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe 435 440 445 Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser 450 455 460

Glu Pro Ile Leu Trp Ile Val Ser Tyr Ala Leu Met Ser Val Cys Gly 475 475 480

Ala Ile Leu Leu Val Leu Ile Val Leu Leu Leu Leu Pro Phe Arg Cys 485 490 495

Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu Ser Ser Leu 500 510

Val Arg His Arg Trp Lys
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<211> 475

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<213> Homo sapiens

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Leu Arg Val Ala Ala Ala Thr Asn Arg Val Val Ala Pro Thr Fro Gly 35 40 45

\* \* \* \* \*

Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu Ala Leu Ala Leu 50 55 60

Glu Pro Ala Leu Ala Ser Pro Ala Gly Ala Ala Asn Phe Leu Ala Met 65 70 75 80

Val Asp Asn Leu Gln Gly Asp Ser Gly Arg Gly Tyr Tyr Leu Glu Met 85 90 95

Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp Thr Gly 100 105 110

Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile Asp Thr 115 120 125

Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly Phe Asp 130 135 140

Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val Gly Glu Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu Val Asn Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly Ile Lys Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys Pro Ser Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser . Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro 

Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr 405 410 415

Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro 420 425 430

Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe 435 440 445

Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser 450 455 460

Glu Pro Ile Leu Trp His His His His His 465 470 475

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Glu Met Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp 35 40 45

Thr Gly Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile 50 55 60

Asp Thr Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly 70 75 80

Phe Asp Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val 85 90 95

Gly Glu Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu 100 105 110

Val Asn Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly 115 120 125

Ile Lys Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys 130 135 . 140

Pro Ser Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser 

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cgctttaagc ttgccaccat gggcgcactg gcccgggcg
                                                                     3.9
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<211> 57
<212> DNA
<213> Artificial sequence
<220>
<223> Primer
cgctttctcg agctaatggt gatggtgatg gtgccacaaa atgggctcgc tcaaaga
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<211>
<212> PRT
<213> Artificial sequence
<220>
<223> Synthetic peptide
<400> 76
Asn Leu Asp Ala
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<212> PRT
<213> Artificial sequence
<220>
<223> Synthetic peptide
<400> 77
Gly Arg Arg Gly Ser
```

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       78
<211>
       6
<212> PRT
<213> Artificial sequence
<220>
<223>
      Synthetic peptide
<400> 78
Thr Gln His Gly Ile Arg
<210> 79
<211>
<212> PRT
<213>
       Artificial sequence
<220>
      Synthetic peptide
<223>
<400> 79
Glu Thr Asp Glu Glu Pro
<210> 80
<211>
      15
<212>
       PRT
<213>
       Artificial sequence
·<220>
<223>
       Synthetic peptide
<400>
       80
Met Cys Ala Glu Val Lys Met Asp Ala Glu Phe Lys Asp Asn Pro
                                    10
                                                        15
<210> 81
<211>
<212> PRT
<213> Artificial sequence
<220>
<223> Synthetic peptide
<400> 81
Asp Ala Glu Phe Arg
<210> 82
<211> 5
<212> PRT
<213> Artificial sequence
```

```
<220>
<223> Synthetic peptide
<400> 82
Ser Glu Val Asn Leu
<210> 83
<211>
<212> PRT
     Artificial sequence
<220>
<223> Peptide of Human APP
<220>
<221> misc_feature
<222>
      (1)
<223> Xaa = Lys or Asn
<220>
<221> misc_feature
<222>
      (2)
<223> Xaa = Met or Leu
<220>
<221> misc_feature
<222> .(3)
<223> Xaa = Asp
<220>
<221> misc_feature
<222> (4)
<223> __Xaa = Asp----
<400> 83
```

Xaa Xaa Xaa Xaa

#### FIGURE 1 (1)

ATGGGCGCACTGGCCGGGCGCTGCTGCTGCTGCTGGCCCAGTGGCTCCTGCGCGCC MGALARALLLPLLAQWLLRA CCCCGGAGCTGGCCCCCCGCGCCCTTCACGCTGCCCCTCCGGGTGGCCGCGCCACGAAC APELAPAPFTLPLRVAAATN CGCGTAGTTGCGCCCACCCCGGGACCCGGGGACCCCTGCCGAGCGCCACGCCGACGGCTTG RVVAPTPGPGTPAERHADGL GCGCTCGCCCTGGAGCCTGCCCTGGCGTCCCCCGCGGGCGCCGCCAACTTCTTGGCCATG ALALEPALASPAGAANFLAM GTAGACAACCTGCAGGGGGACTCTGGCCGCGGCTACTACCTGGAGATGCTGATCGGGACC V D N L Q G D S G R G Y Y L E M L I G T CCCCCGCAGAAGCTACAGATTCTCGTTGACACTGGAAGCAGTAACTTTGCCGTGGCAGGA P P Q K L Q I L V D T G S S N F A V A G ACCCCGCACTCCTACATAGACACGTACTTTGACACAGAGAGGGTCTAGCACATACCGCTCC TPHSYIDTYFDTERSSTYRS AAGGGCTTTGACGTCACAGTGAAGTACACACAAGGAAGCTGGACGGGCTTCGTTGGGGAA K G F D V T V K Y T Q G S W T G F V G E DLVTIPKGFNTSFLVNIATI TTTGAATCAGAGAATTTCTTTTTGCCTGGGATTAAATGGAATGGAATACTTGGCCTAGCT FESENFFLPGIKWNGILGLA TATGCCACACTTGCCAAGCCATCAAGTTCTCTGGAGACCTTCTTCGACTCCCTGGTGACA Y A T L A K P S S S L E T F F D S L V T CAAGCAAACATCCCCAACGTTTTCTCCATGCAGATGTGTGGAGCCGGCTTGCCCGTTGCT Q A N I P N V F S M Q M C G A G L P V A GGATCTGGGACCAACGGAGGTAGTCTTGTCTTGGGTGGAATTGAACCAAGTTTGTATAAA G S G T N G G S L V L G G I E P S L Y K GGAGACATCTGGTATACCCCTATTAAGGAAGAGTGGTACTACCAGATAGAAATTCTGAAA GDIWYTPIKEEWYYQIEILK TTGGAAATTGGAGGCCAAAGCCTTAATCTGGACTGCAGAGAGTATAACGCAGACAAGGCC LEIGGQSLNLDCREYNADKA ATCGTGGACAGTGCCACGCTGCTGCCCCCAGAAGGTGTTTGATGCGGTGGTG IVDSGTTLLRLPQKVFDAVV GAAGCTGTGGCCCGCGCATCTCTGATTCCAGAATTCTCTGATGGTTTCTGGACTGGGTCC EAVARASLIPEFSDGFWTGS CAGCTGGCGTGCTGGACGAATTCGGAAACACCTTGGTCTTACTTCCCTAAAATCTCCATC Q L A C W T N S E T P W S Y F P K I S I TACCTGAGAGATGAGAACTCCAGCAGGTCATTCCGTATCACAATCCTGCCTCAGCTTTAC Y L R D E N S S R S F R I T I L P Q L Y ATTCAGCCCATGATGGGGGCCGGCCTGAATTATGAATGTTACCGATTCGGCATTTCCCCA IQPMMGAGLNYECYRFGISP

TCCACAAATGCGCTGGTGATCGGTGCCACGGTGATGGAGGGCTTCTACGTCATCTTCGAC S T N A L V I G A T V M E G F Y V I F D

AGAGCCCAGAAGAGGGTGGGCTTCGCAGCGAGCCCCTGTGCAGAAATTGCAGGTGCTGCA

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#### FIGURE 1 (2)

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### FIGURE 2 (1)

ATGGCCCAAGCCCTGCCTGGCTCCTGCTGTGGATGGGCGCGGGAGTGCTGCCCAC MAQALPWLLLWMGAGVLPAH GGCACCCAGCACGGCATCCGGCTGCCCCTGCGCAGCGGCCTGGGGGGGCGCCCCCCTGGGG GTQHGIRLPLRSGLGGAPLG CTGCGGCTGCCCCGGGAGACCGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTT LRLPRETDEEPEEPGRRGSF GTGGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGCCAGGGCTACTACGTGGAGATGACC V E M V D N L R G K S G Q G Y Y V E M T GTGGGCAGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTTTGCA VGSPPQTLNILVDTGSSNFA GTGGGTGCTGCCCCCCCCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA V G A A P H P F L H R Y Y Q R Q L S S TACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAG YRDLRKGVYVPYTQGKWEGE LGTDLVSIPHGPNVTVRANI GCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACTGGGAAGGCATCCTG AAITESDKFFINGSNWEGIL GGGCTGGCCTATGCTGAGATTGCCAGGCTTTGTGGTGCTGGCTTCCCCCCTCAACCAGTCT G L A Y A E I A R L C G A G F P L N Q S GAAGTGCTGGCCTCTGTCGGAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTAC EVLASVGGSMIIGGIDHSLY ACAGGCAGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTATGAGGTGATCATTGTG CGGGTGGAGATCAATGGACAGGATCTGAAAATGGACTGCAAGGAGTACAACTATGACAAG RVEINGODLKMDCKEYNYDK AGCATTGTGGACAGTGGCACCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCA SIVDSGTTNLRLPKKVFEAA GTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGA VKSIKAASSTEKFPDGFWLG GAGCAGCTGGTGTGCTGGCAAGCAGCCACCCCCTTGGAACATTTTCCCAGTCATCTCA EQLVCWQAGTTPWNIFPVIS CTCTACCTAATGGGTGAGGTTACCAACCAGTCCTTCCGCATCACCATCCTTCCGCAGCAA LYLMGEVTNQSFRITILPQQ TACCTGCGGCCAGTGGAAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTTTGCCATC

#### FIGURE 2 (2)

YLRPV DVATSODDCYKF E I TCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTC SQSSTGTVMGAVIME G TTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGCCATGTGCACGATGAG F D'R A R K R I G F A V S A C H V H D E TTCAGGACGGCAGCGGTGGAAGGCCCTTTTGTCACCTTGGACATGGAAGACTGTGGCTAC FRTAAVEGPFVTLDMEDCGY AACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATC NIPQTDES TLMTIAYVMAAI TGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGTCAGTGGCGCTGCCTCCGCTGC CALFML CLMVCQWRCLRC PL CTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCCCTGCTGAAGTGAGGAGGCCCA LRQQHDDFADD ISLLK

#### FIGURE 3 (1)

MAQALPWLLLWMGAGVLPAH GGCACCCAGCACGGCATCCGGCTGCCCCTGCGCAGCGGCCTGGGGGGGCGCCCCCCTGGGG G T O H G I R L P L R S G L G G A P L G CTGCGGCTGCCCCGGGAGACCGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGCCAGCTTT LRLPRETDEEPEEPGRRGSF GTGGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACC V E M V D N L R G K S G Q G Y Y V E M T GTGGGCAGCCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTTTGCA VGSPPQTLNILVDTGSSNFA GTGGGTGCTGCCCCCCCCCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA V G A A P H P F L H R Y Y Q R Q L S S T TACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAG YRDLRKGVYVPYTQGKWEGE LGTDLVSIPHGPNVTVRANI GCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACTGGGAAGGCATCCTG AAITESDKFFINGSNWEGIL G L A Y A E I A R P D D S L E P F P D S CTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGGCTTC LVKQTHVPNLFSLQLCGAGF PLNOSEVLASVGGSMIIGGI GACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCCCATCCGGCGGGAGTGGTATTAT DHSLYTGSLWYTPIRREWYY GAGGTCATCATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAAATGGACTGCAAGGAG EVIIVRVEINGQDLKMDCKE TACAACTATGACAAGAGCATTGTGGACAGTGGCACCACCAACCTTCGTTTGCCCAAGAAA YNYDKSIVDSGTTNLRLPKK GTGTTTGAAGCTGCAGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGAT VFEAAVKSIKAASSTEKFPD

#### FIGURE 3 (2)

GGTTTCTGGCTAGGAGCAGCTGGTGTGCTGGCAAGCAGCACCACCCCTTGGAACATT G F W L G E Q L V C W Q A G T T P W N I TTCCCAGTCATCTCACCTAATGGGTGAGGTTACCAACCAGTCCTTCCGCATCACC F P V I S L Y L M G E V T N Q S F R I T ATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTGGCCACGTCCCAAGACGACTGT I L P O O Y L R P V E D V A T S Q D D C TACAAGTTTGCCATCTCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAG YKFAISQSSTGTVMGAVIME GGCTTCTACGTTGTCTTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGC G F Y V V F D R A R K R I G F A V S A C CATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTGTCACCTTGGACATG HVHDEFRTAAVEGPFVTLD GAAGACTGTGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTAT EDCGYNIPOTDESTLMTIAY GTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGTCAGTGG V M A A I C A L F M L P L C L M V C Q W CGCTGCCTCCGCTGCCCCAGCAGCATGATGACTTTGCTGATGACATCTCCCTGCTG RCLRQQHDDFADDISLL AAGTGAGGAGGCCCATGGGCAGAAGATAGAGATTCCCCTGGACCACACCTCCGTGGTTCA K

MAPALHWLLLWVGSGMLPAO GGAACCCATCTCGGCATCCGGCTGCCCCTTCGCAGCGGCCTGGCAGGGCCACCCCTGGGC G T H L G I R L P L R S G L A G P P L G CTGAGGCTGCCCCGGGAGACTGACGAGGAATCGGAGGAGCCTGGCCGGAGAGGCAGCTTT LRLPRETDEESEEPGRRGSF GTGGAGATGGTGGACAACCTGAGGGGGAAAGTCCGGCCAGGGCTACTATGTGGAGATGACC VEMVDNLRGKSGQGYYVEMT GTAGGCAGCCCCCACAGACGCTCAACATCCTGGTGGACACGGGCAGTAGTAACTTTGCA V G S P P Q T L N I L V D T G S S N F A GTGGGGGCTGCCCCACACCCTTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA VGAAPHPFLHRYYQRQLSST TATCGAGACCTCCGAAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAGGGGGAA YRDLRKGVYVPYTQGKWEGE LGTDLVSIPHGPNVTVRANI GCTGCCATCACTGAATCGGACAAGTTCTTCATCAATGGTTCCAACTGGGAGGGCATCCTA AAITESDKFFINGSNWEGIL GGGCTGGCCTATGCTGAGATTGCCAGGCCCGACGACTCTTTGGAGCCCTTCTTTGACTCC G L A Y A E I A R P D D S L E P F F D S CTGGTGAAGCAGACCCACATTCCCAACATCTTTTCCCTGCAGCTCTGTGGCGCTGGCTTC LVKQTHIPNIFSLQLCGAGF PLNQTEALASVGGSMIIGGI GACCACTCGCTATACACGGGCAGTCTCTGGTACACACCCATCCGGCGGGAGTGGTATTAT D H S L Y T G S L W Y T P I R R E W Y Y GAAGTGATCATTGTACGTGGGAAATCAATGGTCAAGATCTCAAGATGGACTGCAAGGAG EVIIVRVEINGQDLKMDCKE TACAACTACGACAAGAGCATTGTGGACAGTGGGACCACCAACCTTCGCTTGCCCAAGAAA YNYDKSIVDSGTTNLRLPKK GTATTTGAAGCTGCCGTCAAGTCCATCAAGGCAGCCTCCTCGACGGAGAAGTTCCCGGAT V F E A A V K S I K A A S S T E K F P D GGCTTTTGGCTAGGGGAGCAGCTGGTGTGCTGGCAAGCAGGCACGACCCCTTGGAACATT G F W L G E Q L V C W Q A G T T P W N I TTCCCAGTCATTTCACTTTACCTCATGGGTGAAGTCACCAATCAGTCCTTCCGCATCACC F P V I S L Y L M G E V T N Q S F R I T ATCCTTCCTCAGCAATACCTACGGCCGGTGGAGGACGTGGCCACGTCCCAAGACGACTGT ILPQQYLRPVEDVATSQDDC TACAAGTTCGCTGTCTCACAGTCATCCACGGGCACTGTTATGGGAGCCGTCATCATGGAA YKFAVSQSSTGTVMGAVIME GGTTTCTATGTCGTCTTCGATCGAGCCCGAAAGCGAATTGGCTTTGCTGTCAGCGCTTGC G F Y V V F D R A R K R I G F A V S A C CATGTGCACGATGAGTTCAGGACGGCGGCAGTGGAAGGTCCGTTTGTTACGGCAGACATG HVHDEFRTAAVEGPFVTADM GAAGACTGTGGCTACAACATTCCCCAGACAGATGAGTCAACACTTATGACCATAGCCTAT EDCGYNIPQTDESTLMTIAY GTCATGGCGCCCATCTGCGCCCTCTTCATGTTGCCACTCTGCCTCATGGTATGTCAGTGG V M A A I C A L F M L P L C L M V C Q W CGCTGCCTGCGTTGCCTGCCCACCAGCACGATGACTTTGCTGATGACATCTCCCTGCTC RCLRCLRHQHDDFADDIS, LL AAGTAAGGAGGCTCGTGGGCAGATGATGGAGACGCCCCTGGACCACATCTGGGTGGTTCC K CTTTGGTCACATGAGTTGGAGCTATGGATGGTACCTGTGGCCAGAGCACCTCAGGACCCT

TGGCGTCATACTCAGGCTACCCGGCATGTGTCCCTGTGGTACCCTGGCAGAGAAAGGGCCAATCTCATTCCCTGCTGGCCAAAGTCAGCAGAAGAAGAAGATTTGCCAGTTGCTTTAGTGATAAGGGACTGCAGACTCAAGCCTACACTGGTACAAAGACTGCGTCTTGAGATAAACAAGAA

]	MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRLPRETDEE	50
1	MAPALHWLLLWVGSGMLPAQGTHLGIRLPLRSGLAGPPLGLRLPRETDEE	50
51	PEEPGRRGSFVEMVDNLRGKSGOGYYVEMTVGSPPOTLNILVDTGSSNFA	100
51	SEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA	100
101	VGAAPHPFLHRYYOROLSSTYRDLRKGVYVPYTOGKWEGELGTDLVSIPH	150
101	VGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPYTQGKWEGELGTDLVSIPH	150
151	GPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDS	200
151	GPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDS	200
201	LVKOTHVPNLFSLOLCGAGFPLNOSEVLASVGGSMIIGGIDHSLYTGSLW	250
201	LVKQTHIPNIFSLQLCGAGFPLNQTEALASVGGSMIIGGIDHSLYTGSLW	250
251	YTPIRREWYYEVIIVRVEINGODLKMDCKEYNYDKSIVDSGTTNLRLPKK	300
251	YTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK	300
301	VFEAAVKSIKAASSTEKFPDGFWLGEOLVCWOAGTTPWNIFPVISLYLMG	350
301	VFEAAVKSIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMG	350
351	EVTNOSFRITILPOOYLRPVEDVATSODDCYKFAISOSSTGTVMGAVIME	400
351	EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQSSTGTVMGAVIME	400
401	GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPOT	450
401	GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTADMEDCGYNIPQT	450
451	DESTLMTIAYVMAAICALFMLPLCLMVCOWRCLRCLRQQHDDFADDISLL	500
451	DESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLL	500
501	K 501	
501	K 501	

#### FIGURE 6 (1)

ATGGCTAGCATGACTGGTGGACAGCAAATGGGTCGCGGATCCACCCAGCACGGCATCCGG MASMTGGQQMGRGSTQHGIR CTGCCCCTGCGCAGCGCCTGGGGGCGCCCCCTGGGGCTGCCCCGGGAGACC LPLRSGLGGAPLGLRLPRET GACGAAGAGCCCGAGGCCGGCCGGAGGGGCAGCTTTGTGGAGATGGTGGACAACCTG DEEPEEPGRRGSFVEMVDNL AGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACCGTGGGCAGCCCCCCGCAGACG RGKSGQGYYVEMTVGSPPQT LNILVDTGSSNFAVGAAPHP TTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACATACCGGGACCTCCGGAAGGGC F L H R Y Y Q R Q L S S T Y R D L R K G GTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAGCTGGGCACCGACCTGGTAAGC V Y V P Y T Q G K W E G E L G T D L V S ATCCCCCATGGCCCCAACGTCACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGAC I P H G P N V T V R A N I A A I T E S D AAGTTCTTCATCAACGGCTCCAACTGGGAAGGCATCCTGGGGCTGGCCTATGCTGAGATT K F F I N G S N W E G I L G L A Y A E I GCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCTCTGGTAAAGCAGACCCACGTT ARPDDSLEPFFDSLVKQTHV CCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGGCTTCCCCCTCAACCAGTCTGAAGTG P\_N L F S L Q L C G A G F P L N Q S E V CTGGCCTCTGTCGGAGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGC LASVGGSMIIGGIDHSLYTG AGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTATGAGGTCATCATTGTGCGGGTG SLWYTPIRREWYYEVIIVRV GAGATCAATGGACAGGATCTGAAAATGGACTGCAAGGAGTACAACTATGACAAGAGCATT EINGQDLKMDCKEYNYDKSI GTGGACAGTGGCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAA VDSGTTNLRLPKKVFEAAVK TCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGAGCAG SIKAASSTEKFPDGFWLGEO CTGGTGTGCTGGCAAGCAGCCACCCCTTGGAACATTTTCCCAGTCATCTCACTCTAC LVCWQAGTTPWNIFPVISLY CTAATGGGTGAGGTTACCAACCAGTCCTTCCGCATCACCATCCTTCCGCAGCAATACCTG LMGEVTNQSFRITILPQQYL CGGCCAGTGGAAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAG

# FIGURE 6 (2)

R P V E D V A T S Q D D C Y K F A I S Q

TCATCCACGGGCACTGTTATGGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTCTTTGAT
S S T G T V M G A V I M E G F Y V V F D

CGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGCCATGTGCACGATGAGTTCAGG
R A R K R I G F A V S A C H V H D E F R

ACGGCAGCGGTGGAAGGCCCTTTTGTCACCTTGGACATGAGACTGTGGCTACAACATT
T A A V E G P F V T L D M E D C G Y N I

CCACAGACAGATGAGTCATGA
P Q T D E S \*

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#### FIGURE 7 (1)

ATGGCTAGCATGACTGGTGGACAGCAAATGGGTCGCGGATCGATGACTATCTCTGACTCT MASMTGGQQMGRGSMTISDS CCGCGTGAACAGGACGGATCCACCCAGCACGGCATCCGGCTGCCCCTGCGCAGCGGCCTG P R E Q D G S T Q H G I R L P L R S G L GGGGGCGCCCCCTGGGGCTGCCCCGGGAGACCGACGAGAGCCCGAGGAGCCC GGAPLGLRLPRETDEEPEEP GGCCGGAGGGCAGCTTTGTGGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGCAGGGC G R R G S F V E M V D N L R G K S G Q G TACTACGTGGAGATGACCGTGGGCAGCCCCCGCAGACGCTCAACATCCTGGTGGATACA YYVEMTVGSPPQTLNILVDT G S S N F A V G A A P H P F L H R Y Y Q AGGCAGCTGTCCAGCACATACCGGGACCTCCGGAAGGGCGTGTATGTGCCCTACACCCAG RQLSSTYRDLRKGVYVPYTO GGCAAGTGGGAAGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCCATGGCCCCAACGTC G K W E G E L G T D L V S I P H G P N V ACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCC TVRANIAAITESDKFFINGS AACTGGGAAGGCATCCTGGGGCTGGCCTATGCTGAGATTGCCAGGCCTGACGACTCCCTG NWEGILGLAYAEIARPDDSL GAGCCTTTCTTTGACTCTCTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAG E P F F D S L V K Q T H V P N L F S L Q LCGAGFPLNQSEVLASVGGS ATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCCATC MIIGGIDHSLYTGSLWYTPI CGGCGGGAGTGGTATTATGAGGTCATCATTGTGCGGGTGGAGATCAATGGACAGGATCTG R R E W Y Y E V I I V R V E I N G Q D L AAAATGGACTGCAAGGAGTACAACTATGACAAGAGCATTGTGGACAGTGGCACCAAC KMDCKEYNYDKSIVDSGTTN CTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAATCCATCAAGGCAGCCTCCTCC LRLPKKVFEAAVKSIKAASS ACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGC T E K F P D G F W L G E Q L V C W Q A G ACCACCCCTTGGAACATTTTCCCAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAAC TTPWNIFPVISLYLMGEVTN

### FIGURE 7 (2)

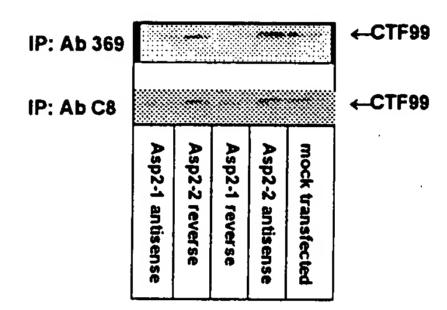
#### FIGURE 8 (1)

ATGACTCAGCATGGTATTCGTCTGCCACTGCGTAGCGGTCTGGGTGGTGCTCCACTGGGT MTQHGIRLPLRSGLGGAPLG CTGCGTCTGCCCCGGGAGACCGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTT LRLPRETDEEPEPGRRGSF GTGGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGCCAGGGCTACTACGTGGAGATGACC V E M V D N L R G K S G Q G Y Y V E M T GTGGGCAGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTTTGCA V G S P P Q T L N I L V D T G S S N F A GTGGGTGCTGCCCCCCCCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA V G A A P H P F L H R Y Y Q R Q L S S T TACCGGGACCTCCGGAAGGGGCTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAG YRDLRKGVYVPYTQGKWEGE LGTDLVSIPHGPNVTVRANI GCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACTGGGAAGGCATCCTG AAITESDKFFINGSNWEGIL G L A Y A E I A R P D D S L E P F F D S CTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGCTTC LVKQTHVPNLFSLQLCGAGF PLNQSEVLASVGGSMIIGGI -GACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTAT DHSLYTGSLWYTPIRREWYY GAGGTCATCATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAAATGGACTGCAAGGAG E V I I V R V E I N G Q D L K M D C K E TACAACTATGACAAGAGCATTGTGGACAGTGGCACCACCAACCTTCGTTTGCCCAAGAAA YNYDKSIVDSGTTNLRLPKK -GTGTTTGAAGCTGCAGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGAT V F E A A V K S I K A A S S T E K F P D -GGTTTCTGGCTAGGAGCAGCTGGTGTGCTGGCAAGCAGCCACCCCCTTGGAACATT G F W L G E Q L V C W Q A G T T P W N I -TTCCCAGTCATCTCACCTAATGGGTGAGGTTACCAACCAGTCCTTTCGCATCACC FPVISLYLMGEVTNQSFRIT -ATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTGGCCACGTCCCAAGACGACTGT I L P Q Q Y L R P V E D V A T S Q D D C -

No Brown

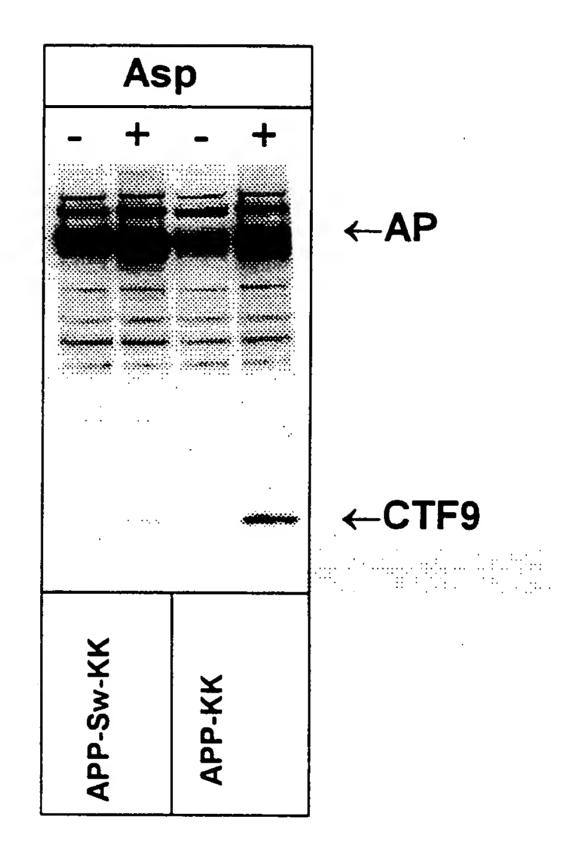
## FIGURE 8 (2)

TACAAGTTTGCCATCTCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAG
Y K F A I S Q S S T G T V M G A V I M E 
GGCTTCTACGTTGTCTTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGC
G F Y V V F D R A R K R I G F A V S A C 
CATTAG
H \*



1. 30°

FIGURE 10



MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRLPRETDEE PEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA VGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPYTQGKWEGELGTDLVSIPH GPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDS LVKQTHVPNLFSLQLCGAGFPLNQSEVLASVGGSMIIGGIDHSLYTGSLW YTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK VFEAAVKSIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMG EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQT DES

MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRLPRETDEE PEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA VGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPYTQGKWEGELGTDLVSIPH GPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDS LVKQTHVPNLFSLQLCGAGFPLNQSEVLASVGGSMIIGGIDHSLYTGSLW YTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK VFEAAVKSIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMG EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQT DESHHHHHH

20/20

1. 30